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Breast Cancer Detection by Preoperative Imaging in Reduction Mammoplasty Patients: A Single Center Study of 918 Patients

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Abstract

Background The role of preoperative imaging and the usability of different imaging modalities is highly variable and controversial in reduction mammoplasty patients. Our study describes the imaging process in a single center in regard to modality selection, age and timing, and of the association between imaging and histopathological findings in reduction mammoplasty specimens.

Methods Nine hundred eighteen women, who underwent reduction mammoplasty during 1.1.2007–31.12.2011, were retrospectively reviewed for demographics, preoperative imaging, further preoperative examinations, and pathology reports.

Results Preoperative imaging had been conducted for 89.2% ($n = 819$) of the patients. In 49 (6.0%) patients, suspicious preoperative imaging led to further examinations revealing 2 high-risk lesions (atypical ductal hyperplasia (ADH), lobular carcinoma in situ (LCIS)), and 2 cancers preoperatively. Postoperatively abnormal histopathology specimens were revealed in 88 (10.4%) patients. The incidence of high-risk lesions was 5.5% ($n = 47$), and the incidence of cancer was 1.2% ($n = 10$). Preoperative imaging was normal (BI-RADS 1 and BI-RADS 2) in 80.8% of these patients. The sensitivity of the preoperative imaging for cancer detection was 20.0%, and the specificity was 100.0%.

Conclusions Preoperative imaging and further examinations do not sufficiently detect malignant or cancer risk-increasing findings. Therefore, histopathological analysis of reduction mammoplasty specimens seems mandatory.

Introduction

Reduction mammoplasty is a common procedure in plastic surgery. Indications for this surgery are symptomatic macromastia, breast asymmetry, and contralateral breast symmetrisation during or after breast cancer surgery. Breast cancer is the most frequent cancer among women, the lifetime risk being 1 in 8. It is thus unsurprising that incidental cancers, in situ findings, and benign breast disease demonstrating increased risk of breast cancer are revealed in the process of reduction mammoplasty.

The incidence of occult breast cancer in reduction mammoplasty specimens has been under study in several countries with incidences ranging from 0.05 to 4.5 percent

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Table 1 BI-RADS classification

Category	Definition	Likelihood of cancer
BI-RADS 0	Incomplete	N/A
BI-RADS 1	Negative	Essentially 0%
BI-RADS 2	Benign	Essentially 0%
BI-RADS 3	Probably benign	>0%, but \leq 2%
BI-RADS 4	Suspicious	>2%, but <95%
BI-RADS 5	Highly suggestive of malignancy	\geq 95%
BI-RADS 6	Known biopsy-proven malignancy	N/A

[1–9]. Studies also indicate that women with benign breast disease, commonly detected in reduction mammoplasty specimens, are at higher risk for breast cancer [2, 3, 10–17].

The question of routine preoperative imaging in reduction mammoplasty is an ongoing one, which we have not yet come to a consensus. Mammogram is variously recommended for different age groups [1, 3, 5, 7, 8, 12, 18–21].

The present study aims to retrospectively describe the use of different imaging modalities. The association between preoperative imaging, needle biopsies, and final histopathological findings in reduction mammoplasty patients is described.

Materials and methods

A total of 1255 women underwent reduction mammoplasties during 1.1.2007–31.12.2011. Patients with previous history of breast cancer were excluded and the remaining patients amounting to 918. The indications for the surgery were symptomatic macromastia or asymmetry of the breasts. Unilateral procedures were performed in 35 cases due to congenital or postoperative asymmetry. Findings were recorded per individual and not per breast. Retrospective electronic and paper records were retrieved. Demographic data, results of preoperative imaging, operative and pathology reports, and postoperative follow-up were recorded. The study was approved by the University Hospital Research Board.

During the study period, imaging protocols varied. Ultrasound, mammogram, or both imaging modalities were conducted depending which was the imaging site, breast density, and age. Some patients were referred to conduct imaging in the private sector or in primary healthcare centers. Some patients did not undergo any preoperative imaging. The different approaches to imaging were due to present routines, and thus, the groups were not designed for research purposes.

Preoperative imaging findings were retrospectively classified according to the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS)

[22]. This classification is presented in Table 1. In our study, BI-RADS 1 and BI-RADS 2 were categorized as normal breast imaging findings and BI-RADS 3 and BI-RADS 4 as suspicious of malignancy. Breast density was retrospectively analyzed for patients with malignant postoperative histopathology according to BI-RADS lexicon [22].

For histopathological analysis, reduction mammoplasty specimens were weighed, formalin fixed, and cut into 1-cm slices that were palpated for masses and for areas of increased density. Samples for blocks were taken from macroscopically suspicious areas and analyzed histopathologically. The number of blocks per breast varied between 4 and 20, 5 being the most usual amount.

We categorized abnormal histopathological findings in reduction mammoplasty specimens based on a consensus statement outlined by the Cancer Committee of the College of American Pathologists in 1985 and incorporated the 1998 consensus statement update [16]. In short, high-risk lesions included atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), and lobular carcinoma in situ (LCIS). Invasive cancer and ductal carcinoma in situ (DCIS) were classified as cancer findings.

We retrospectively studied if the findings in preoperative imaging associated with histopathological diagnosis of the specimens. Those patients who had malignant postoperative histopathology had their mammogram reviewed and re-analyzed by radiologist (K.H.) with 10 years of breast imaging experience. We also registered the time frame in which patients had completed preoperative imaging prior to surgery, and 6 months or less was considered as a cutoff according to the present recommendation.

Descriptive statistics were reported as the mean value and range between minimum and maximum. Pearson's Chi-squared test was applied in bivariate analyses with categorical variables. Two-sample *t* test and analysis of variance were used when patient age was compared between patient groups. The sensitivity of preoperative imaging and diagnosis was calculated as cancers detected preoperatively compared to all cancers diagnosed in reduction mammoplasty specimens. The specificity was calculated as patients with normal preoperative imaging compared to patients without cancer in their specimens.

Table 2 Preoperative imaging

Imaging modality	Patients (%)	Mean age and range
Mammogram alone	250 (27.2%)	47.0 (18–73)
Ultrasound alone	15 (1.6%)	21.5 (18–26)
Both modalities	554 (60.3%)	43.8 (18–79)
No imaging	99 (10.8%)	43.2 (16–68)

Results

A total of 918 women underwent reduction mammoplasty with a mean age of 44.3 years (range 16–79 years) and a mean body mass index of 27.7 (range 19.0–50.5). Preoperative imaging had been conducted for 89.2% of the patients ($n = 819$). The different imaging modalities and the number of patients are presented in Table 2. The mean age of the patients with normal (BI-RADS 1 and BI-RADS 2) imaging findings did not statistically differ from patients with imaging suspicious of malignancy (BI-RADS 3 and BI-RADS 4).

Association between BI-RADS class of mammogram and ultrasound

Among the patients with both imaging modalities ($n = 554$), BI-RADS classes of mammogram and ultrasound coincided in 536 (96.8%) of the patients. For 18 patients (aged 32–67 years), additional ultrasound revealed suspicious lesions, which were undetectable in mammogram. These lesions were biopsied ($n = 15$) with benign results, or surgical open biopsy ($n = 2$) was performed simultaneously with reduction mammoplasty. Final histopathology revealed high-risk lesions in 5 patients. One patient had no further work-up despite BI-RADS 4 class in the ultrasound (left breast), and the final histopathology revealed DCIS in both breasts, sized 7 mm (right breast) and 2.5 mm (left breast).

Preoperative further examinations

In total, BI-RADS 3 and BI-RADS 4 category in preoperative imaging was found in 56 (6.8%) patients of the 819 imaged. In 12 of these patients, no further examinations were performed. In 49 of 819 (6.0%) patients, imaging led to further examinations. The mean age of these patients was 45.3 years (range 23–67 years). Mammographic magnification of suspicious area had been conducted for 9 patients. Figure 1 shows the process of patients needing biopsies. In total, further examinations revealed 2 cancers (48 and 58 years), 1 ADH (50 years), and 1 LCIS

(56 years) finding. Table 3 demonstrates features and treatment of 2 preoperatively diagnosed cancer findings.

Histopathology

Histopathologically abnormal findings in reduction mammoplasty specimens were revealed in 88 (10.4%) patients. The incidence of high-risk lesions was 5.5% ($n = 47$). In 69 (7.5%) patients, no sample was taken for histopathological analysis. In patients with abnormal histopathology, preoperative imaging had been conducted for 78 (88.6%) patients and no imaging was performed for 10 (11.4%) patients. Preoperative imaging was normal (BI-RADS 1 and BI-RADS 2) in 80.8% and suspicious of malignancy (BI-RADS 3 and BI-RADS 4) in 19.2% of these patients.

Among patients ($n = 56$) with imaging suspicious of malignancy (BI-RADS 3 and BI-RADS 4), reduction mammoplasty specimens revealed abnormal histopathological findings in 27.3% and normal findings in 72.7% of the patients. One patient had no histopathological analysis of reduction mammoplasty specimen despite suspicious imaging. During the study period, no mention of subsequent oncological incident was found with this patient.

Final histopathology revealed 10 (1.2%) patients with invasive cancer or DCIS. The mean age of the patients was 55.5 years (range 48–67 years). The features of preoperatively undetected cancer findings are demonstrated in Table 4.

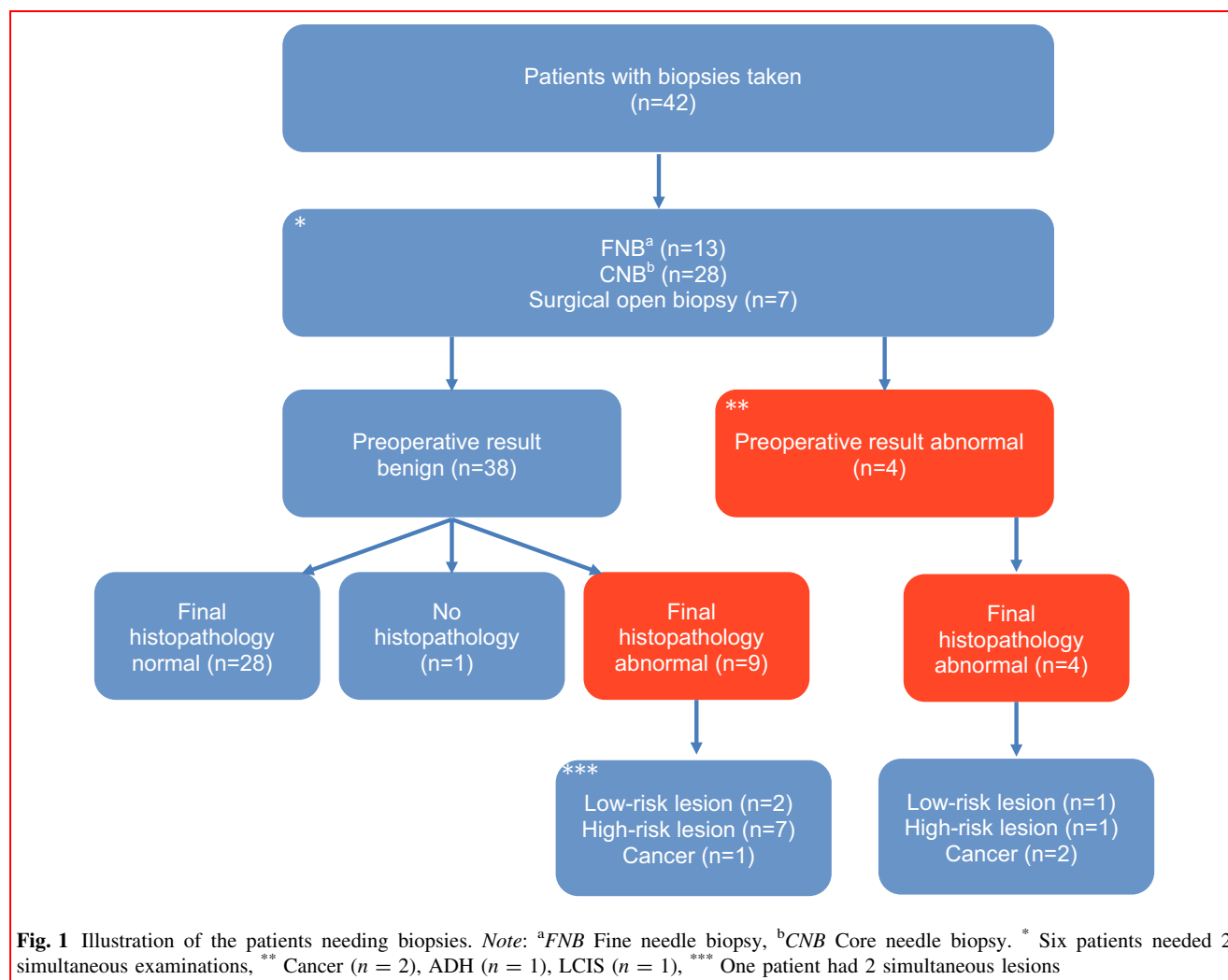
Preoperative imaging of the 10 patients with malignant histopathology was retrospectively searched for, and 8 were retrieved and re-analyzed by an experienced radiologist. None of the previously undetected cancer findings could be identified retrospectively.

Sensitivity and specificity of imaging

The sensitivity of the preoperative imaging was 20.0%, considering that the final histopathology encompasses only the operated part of the breast. There were no false-positive preoperative biopsy findings leading to specificity of 100.0%.

Timing of imaging

The date of imaging could be retrieved from patient records in 738 cases. The number of patients with conducted imaging within 6 months prior to surgery was 699 (94.7%), and the number of patients with older imaging was 39 (5.3%). Abnormal histopathological findings were detected in 9.7% in the timely imaged group and in 12.8% in the group with older imaging (ns).

**Table 3** Preoperatively diagnosed cancer findings

Patient	Imaging	Tumor size in imaging	Needle biopsy	Treatment	Tumor size in histopathology
Patient 1	MMG ^a (BI-RADS 4), US ^b (BI-RADS 4) D2 ^c	14 mm (MMG, US)	CNB ^d	Oncoplastic resection, SNB ^e , contralateral reduction mammoplasty	13 mm
Patient 2	MMG (BI-RADS 2, 4), US (BI-RADS 4) D1	11 mm (MMG), 10 × 7 × 7 mm (US)	CNB	Oncoplastic resection, SNB, contralateral reduction mammoplasty	12 mm

^a MMG mammogram^b US ultrasound^c D breast density^d CNB core needle biopsy^e SNB sentinel node biopsy

Discussion

Preoperative imaging before reduction mammoplasty remains controversial, as no consensus exists. Our study allows analysis of the imaging process in regard to

modality selection, age and timing, and of the association between imaging and histopathological findings in reduction mammoplasty specimens.

In our study, the imaging protocol differed between imaging sites. One imaging center conducted mammogram

Table 4 Preoperatively undetected cancer findings in reduction mammoplasty specimens

Patient	Age	Imaging modality	Further examinations	Result	Histopathological diagnosis of the specimen	Size of cancer
1	51	MMG ^a , US ^b D2 ^c	FNB ^d , CNB ^e	Benign	Carcinoma ductale	40 mm
2	51	MMG, US D3	None	–	DCIS ^f (both breasts)	7 mm (right) 2,5 mm (left)
3	49	MMG, US D3	None	–	DCIS (right) Carcinoma lobulare (left)	2 mm (right) 7 lesions, 2–6 mm (left)
4	50	MMG, US D2	None	–	Carcinoma lobulare, DCIS	7 mm (cancer) unknown (DCIS)
5	67	MMG D1	None	–	Carcinoma ductale	7 mm
6	57	MMG D3	None	–	DCIS	2 mm
7	62	MMG D2	None	–	DCIS	11 mm + 7 mm
8	62	None	None	–	DCIS	2 mm

^a MMG mammogram^b US ultrasound^c D breast density^d FNB fine needle biopsy^e CNB core needle biopsy^f DCIS ductal carcinoma in situ

and ultrasound for the majority of the patients regardless of age. Another center conducted ultrasound for women under 28 years and mammogram for older with additional ultrasound in case of dense breasts or suspicious findings in mammogram. A group of patients were asked to conduct imaging in the private sector or in primary healthcare centers. In 10.8% of the patients, with a mean age of 43.2 years, neither of the imaging modalities was completed or the information about imaging could not be confirmed. Younger patients may symbolize low-cancer-risk patients, but this does not explain the lack of imaging in older patients. Pending information on imaging may be due to a large amount of patients who conduct imaging in the private sector with no mention about imaging in the patient records. This focuses attention on the importance of a preoperative routine.

In the literature, variation exists between imaging protocols in different countries. In the UK, 92% of breast surgeons and 41% of plastic surgeons routinely performed radiological screening for reduction mammoplasty patients. The majority chose age as an indicator for screening [21]. In the Netherlands [18], only 3% of the responders to a survey routinely required preoperative mammogram, and only 1 responder routinely required preoperative ultrasound. In general, preoperative mammogram is variously recommended from the age of 30 [12], from the age of 40 [3, 5, 18, 23, 24], or for patients over the age of 50 [19]. In our study, patients were imaged in all age groups, the mean age of these patients being over 40 years.

Reduction mammoplasty changes the architecture of the breast. In case of incidental cancer, breast-conserving

options may be limited. Therefore, emphasis should be placed on preoperative diagnosis [23, 24]. In our study, 80.8% of the patients with abnormal findings in reduction mammoplasty specimens had normal preoperative imaging. Similarly, others [3, 5–7, 20] have noticed that incidental discovery of atypical hyperplasia, LCIS, or cancer were not associated with abnormal imaging. Moreover, only 2 out of 10 cancers in our study were detected preoperatively. It seems that preoperative imaging does not sufficiently detect high-risk or cancer findings. Therefore, histopathological analysis of reduction mammoplasty specimens seems difficult to bypass.

Among the preoperatively undetected cancers, 1 patient (carcinoma ductale 40 mm) had fine and core needle biopsies taken with benign results. Either biopsies were targeted incorrectly, or more likely preoperative histopathology was suboptimized. In 3 patients, both mammogram and ultrasound were unable to detect cancer or DCIS preoperatively despite bilateral malignancies in 2 of them. Growth pattern of DCIS and lobular cancer, as well as small size, may explain why these lesions were undetectable. In 3 patients with malignant outcome, preoperative mammogram alone, with breast densities varying from D1 to D3, was conducted. In theory, the false-negative ductal cancer, sized 7 mm, might have been found with additional ultrasound. In 1 patient, no preoperative imaging was conducted, which precludes the possibility of preoperative diagnostics. Nevertheless, small invasive cancers, DCIS, or high-risk lesions may remain undetected with all imaging modalities, including MRI. In our study, the sensitivity of the imaging was 20.0%. It can be explained by small size of undetected cancers. The

specificity in our study was 100.0%. There were no false-positive cancers.

Our study revealed 18 patients with incoherent imaging. Despite normal mammogram, ultrasound was performed and showed BI-RADS 4 unexpectedly. Eventually, 33.3% of the patients had either DCIS or a high-risk lesion in the specimens. Although actual cancer findings in the reduction mammoplasty specimens were rare in this patient group, a considerable amount of findings indicating increased risk of breast cancer were detected. Benign breast disease is an important predictor of future breast cancer risk [10–17]. High-risk lesions, including ADH and ALH, cause moderately increased risk (4.0–5.0 times), and LCIS causes markedly increased risk (8.0–10.0 times) of breast cancer [16]. In screening situations [25], patients with a history of ADH or ALH, or LCIS may benefit from adjunct (ultrasound or MRI) screening due to lower mammogram specificity and higher interval cancer rates. However, in our study, a substantial amount of work with false-positive imaging raises the question of the use of routine ultrasound in combination with mammogram, as opposed to ultrasound only in dense breasts or additionally to suspicious mammogram. Based on our results, it remains to be elucidated if both ultrasound and mammogram are needed.

The importance of screening mammogram has been debated lately and guidelines re-assessed. Also, there are differences in target age between countries. Currently, routine mammographic screening is not recommended for women under the age of 40. Sensitivity of mammogram is lower among young women and in dense breasts [26]. However, breast cancers in very young women are typically aggressive [27], and DCIS in young women is often multifocal and multicentric [28]. These studies support preoperative imaging also in very young women. Based on this, prior to major breast surgery changing the architecture of the breast, we recommend preoperative ultrasound for women under 30 years of age in our unit, and mammogram is recommended for patients older than that. There are no national guidelines available. In our study, a large number of patients ($n = 819$) conducted imaging with only 2 cancers and 2 high-risk lesions detected preoperatively. Still, these operations could be planned and performed as oncoplastic resections, which supports the role of preoperative imaging. On the other hand, all other abnormalities went undetected in the imaging. This highlights the value of histopathological analysis as the method to detect cancer and risk-increasing lesions.

We acknowledge some limitations to our study. In a large institution and between facilities, breast imaging and the threshold to conduct additional imaging or examinations may vary. Also, patients requiring mastectomy or more extensive oncological treatment may have been referred to Breast Unit, and therefore, the data are missing

from our material. The study is retrospective, which compels us to rely on record keeping of others. The time period between surgery and data collection is limited. It remains uncertain, if the unoperated part of the breast contains cancer or risk-increasing findings. Therefore, the sensitivity of mammogram is calculated for the operated part of the breast, and the true sensitivity may be even lower. In 99 patients, it was not possible to discern between missing preoperative imaging and missing data.

In conclusion, emphasis should be placed on the quality and documentation of preoperative evaluation of reduction mammoplasty patients. To date, preoperative imaging and further examinations do not sufficiently detect cancer or high-risk lesions; therefore, histopathological evaluation of reduction mammoplasty specimens seems mandatory.

Compliance with ethical standards

Conflicts of interest All authors have no conflicts of interest to declare.

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